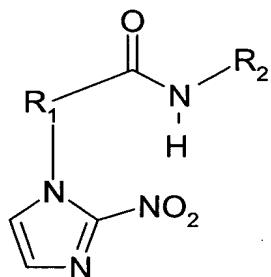


This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

Claim 1 - 5 (canceled)

Claim 6 (previously presented) A method for the synthesis of a [¹⁸F]-labeled perfluorinated-nitroaromatic compound having the formula:



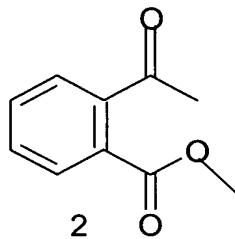
wherein R₁ is CH₂ and R₂ is an alkyl group having up to about 6 halogen atoms, wherein said alkyl group has the formula CHXCX₂CY₃ where X is halogen or hydrogen and Y is fluorine, comprising

(1) perfluorinating a first intermediate which is an amino acid derivative which is N-protected by an imido group or a synthetically equivalent group having a carboxyl function transformed into a dithioester function or a synthetically equivalent persulphurated moiety thereby obtaining a [¹⁸F]-labeled perfluorinated amino acid derivative which is N-protected by an imido group or a synthetically equivalent group as a second intermediate and

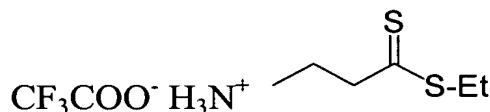
(2) deprotecting the nitrogen function of said second intermediate, resulting in a [¹⁸F] labeled perfluoroalkyl amine derivative, and coupling 2-(2-nitro-imidazol-1-yl) acetic acid with a [¹⁸F] labeled perfluoroalkyl amine derivative.

Claim 7 (currently amended) A method for the synthesis of a compound according to claim 6, wherein step (1) comprises comprising:

a) adding a THF solution of a compound of formula 2 to a suspension of PYBOP in THF followed by Et₃N,



b) adding an amine of formula 1 and Et₃N to the solution obtained in step (a),



c) adding a catalytic amount to the solution obtained in step (b) of pTsOH and refluxing the solution,

d) cooling the solution obtained after step (c) at ambient temperature and adding a sodium bicarbonate solution,

e) extracting the product obtained after step (d) with ethyl acetate and drying and concentrating the product with ethyl acetate,

f) purifying the residue obtained after step (e) by column chromatography on silica gel,

g) removing traces of water by washing the product of step (f) with trifluoroacetic anhydride,

h) reacting a persulphurated derivative obtained from step (g) with a suitable labeled perfluorinating agent and a suitable oxidant resulting in a compound having a high yield of fluorine fluor atom incorporation,

and wherein step (2) comprises:

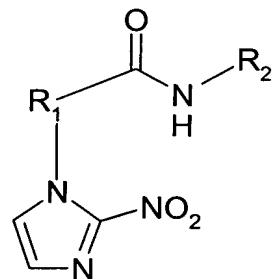
- i) deprotecting the nitrogen function, resulting in a perfluoroalkyl amine derivative, and
- j) coupling the perfluoroalkyl amine derivative obtained in step (i) with an activated form of 2-(2-nitro-imidazol-1-yl) acetic acid, resulting in the $[18\text{F}]$ -labeled or perfluorinated-nitroaromatic compound.

Claim 8 (currently amended) A method according to claim 7 wherein hydrogen fluoride/pyridine complex (HF-Pyridine) is used as a perfluorinating agent and 1,3-dibromo-5,5-dimethylhydantoin (DBH) is used as an oxidant resulting in a compound having a high yield of fluorine ~~fluo~~ atom incorporation.

Claims 9 - 25 (canceled)

Claim 26 (currently amended) A method for the detection of tissue hypoxia in a patient comprising:

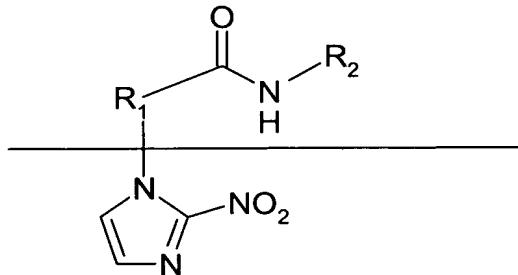
- producing ~~according to the method of claim 6~~ a $[18\text{F}]$ -labeled perfluorinated-nitroaromatic compound having the formula:



wherein R₁ is CH₂ and R₂ is an alkyl group having up to about 6 halogen atoms, wherein said alkyl group has the formula CH_XCX₂ CY₃ where X is halogen or hydrogen and Y is fluorine by (1) perfluorinating a first intermediate which is an amino acid derivative which is N-protected by an imido group or a synthetically equivalent group having a carboxyl function

transformed into a dithioester function or a synthetically equivalent persulphurated moiety thereby obtaining a [¹⁸F]-labeled perfluorinated amino acid derivative which is N-protected by an imido group or a synthetically equivalent group as a second intermediate and

(2) deprotecting the nitrogen function of said second intermediate, resulting in a [¹⁸F] labeled perfluoroalkyl amine derivative, and coupling 2-(2-nitro-imidazol-1-yl) acetic acid with a [¹⁸F] labeled perfluoroalkyl amine derivative coupling 2-(2-nitro-imidazol-1-yl) acetic acid with a [¹⁸F] labeled perfluoroalkyl amine derivative according to the method of claim 6;

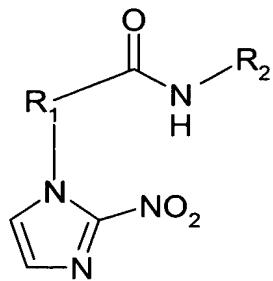


and - quantifying tissue hypoxia in said patient by imaging said patient after having introduced said [¹⁸F] labeled nitromidazole compound into said patient.

Claim 27 (original) A method according to claim 26 wherein the detection technique used in said method is positron emission tomography.

Claim 28 (currently amended) A method for the detection of tissue hypoxia in a tissue comprising:

- producing according to the method of claim 6 a [¹⁸F]-labeled perfluorinated-nitroaromatic compound having the formula:



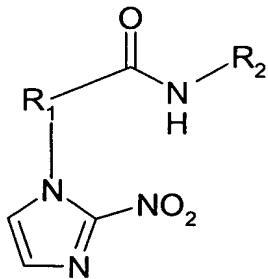
wherein R₁ is CH₂ and R₂ is an alkyl group having up to about 6 halogen atoms, wherein said alkyl group has the formula CH_XCX₂ CY₃ where X is halogen or hydrogen and Y is fluorine by (1) perfluroinating a first intermediate which is an amino acid derivative which is N-protected by an imido group or a synthetically equivalent group having a carboxyl function transformed into a dithioester function or a synthetically equivalent persulphurated moiety thereby obtaining a [¹⁸F]-labeled perfluorinated amino acid derivative which is N-protected by an imido group or a synthetically equivalent group as a second intermediate and

(2) deprotecting the nitrogen function of said second intermediate, resulting in a [¹⁸F] labeled perfluoroalkyl amine derivative, and coupling 2-(2-nitro-imidazol-1-yl) acetic acid with a [¹⁸F] labeled perfluoroalkyl amine derivative coupling 2-(2-nitro-imidazol-1-yl) acetic acid with a [¹⁸F] labeled perfluoroalkyl amine derivative;

- introducing said [¹⁸F] labeled nitroimidazole compound of claim 6 into a patient,
- removing a tissue sample from said patient, and
- analysing the emission in said tissue sample by autoradiography.

Claim 29 (currently amended) A method for the detection of an [¹⁸F] labeled bioactive compound in a patient comprising:

- producing according to the method of claim 6 a [¹⁸F]-labeled perfluorinated-nitroaromatic compound having the formula:



wherein R₁ is CH₂ and R₂ is an alkyl group having up to about 6 halogen atoms, wherein said alkyl group has the formula CH_XCX₂ CY₃ where X is halogen or hydrogen and Y is fluorine by (1) perfluorinating a first intermediate which is an amino acid derivative which is N-protected by an imido group or a synthetically equivalent group having a carboxyl function transformed into a dithioester function or a synthetically equivalent persulphurated moiety thereby obtaining a [¹⁸F]-labeled perfluorinated amino acid derivative which is N-protected by an imido group or a synthetically equivalent group as a second intermediate and

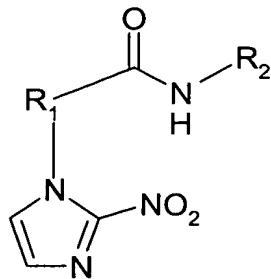
(2) deprotecting the nitrogen function of said second intermediate, resulting in a [¹⁸F] labeled perfluoroalkyl amine derivative, and coupling 2-(2-nitro-imidazol-1-yl) acetic acid with a [¹⁸F] labeled perfluoroalkyl amine derivative ~~coupling 2-(2-nitro-imidazol-1-yl) acetic acid with a [¹⁸F] labeled perfluoroalkyl amine derivative;~~

- introducing said [¹⁸F] labeled bioactive compound according to claim 6 into said patient,

- imaging the presence of said [¹⁸F] labeled bioactive compound in said patient, and -optionally, quantifying the presence of said [¹⁸F] labeled bioactive compound in said patient.

Claim 30 (currently amended) A method for the detection of [¹⁸F] labeled bioactive compound in a tissue comprising:

- producing according to the method of claim 6 a [¹⁸F]-labeled perfluorinated-nitroaromatic compound having the formula:



wherein R₁ is CH₂ and R₂ is an alkyl group having up to about 6 halogen atoms, wherein said alkyl group has the formula CHX₂ CY₃ where X is halogen or hydrogen and Y is fluorine by (1) perfluroinating a first intermediate which is an amino acid derivative which is N-protected by an imido group or a synthetically equivalent group having a carboxyl function transformed into a dithioester function or a synthetically equivalent persulphurated moiety thereby obtaining a [¹⁸F]-labeled perfluorinated amino acid derivative which is N-protected by an imido group or a synthetically equivalent group as a second intermediate and

(2) deprotecting the nitrogen function of said second intermediate, resulting in a [¹⁸F] labeled perfluoroalkyl amine derivative, and coupling 2-(2-nitro-imidazol-1-yl) acetic acid with a [¹⁸F] labeled perfluoroalkyl amine derivative coupling 2-(2-nitro-imidazol-1-yl) acetic acid with a [¹⁸F] labeled perfluoroalkyl amine derivative;

- introducing an [¹⁸F] labeled bioactive compound of claim 6 into a patient,
- taking a tissue sample from said patient, and
- analysing the emission in said tissue sample by autoradiography.

Claim 31 (canceled)

Claim 32 (currently amended) A method according to claim 6, wherein the compound has a specific radioactivity of 1 to 30 Ci/mmol.

Claim 33 (currently amended) A method according to claim 6, wherein the compound has the formula 2-(2-nitro-1H-imidazol-1-yl)-N-(3,3,3-trifluoropropyl) acetamide ([¹⁸F]-EF3).

Claim 34 (currently amended) A method according to claim 6, wherein the compound ~~is has the formula~~ 2(2-nitro-1H-imidazol-1-yl)-N-2,2,3,3,3-pentafluoropropyl) acetamide ($[^{18}\text{F}]$ -EF5).

Claim 35 (canceled)